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Synthesis of [1,2,4]Triazolo[1,5-*c*]pyrimidine Derivatives

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Condensation of diaminomethylenehydrazones with ethoxymethylenemalononitrile (**2**) gave 2,3-dihydro[1,2,4]triazolo[1,5-*c*]pyrimidines in moderate to high yields. Of the variously substituted diaminomethylenehydrazones, amino(monosubstituted amino)methylene ones were most reactive in this condensation, regardless of the nature of the 4-substitutent. The reaction was found to be initiated at N-3 by attack on the ethoxymethine carbon of **2**, followed by an electrocyclic reaction to form the bicyclic pyrimidine. The 2,3-dihydro compounds were oxidized with iron(III) chloride in aqueous acetic acid or iodine in ethyl alcohol to give the corresponding [1,2,4]triazolo[1,5-*c*]pyrimidines.

Keywords——diaminomethylenehydrazone; ethoxymethylenemalononitrile; amino(dicyanovinylamino)methylenehydrazone; 2,3-dihydro[1,2,4]triazolo[1,5-*c*]pyrimidine; [1,2,4]triazolo[1,5-*c*]pyrimidine

Diaminomethylenehydrazones, including those employed in the present study as starting materials, have long been known.[1] Investigations of diaminomethylenehydrazones have been primarily focused on the pharmaceutical aspects, with the aim of finding new drugs of chemotherapeutic value[2] and little work has been done on their use as reagents[3] for synthetic purposes in heterocyclic chemistry.

Diaminomethylenehydrazones are considered to be polyfunctional nucleophiles and are expected to show different nucleophilicities at the different nitrogens. In fact, it is known[4] that the internal nitrogen (N-2)[5] preferentially attacks an alkyl halide to displace the halide ion and it seems to be a softer center than the terminal nitrogens (N-3, N-4). By selecting appropriate electrophiles, it is expected that diaminomethylenehydrazones may prove to be useful as reagents for the synthesis of new heterocycles.

Recently, it has been reported[6] that 4-unsubstituted isothiosemicarbazones readily react with ethoxymethylenemalononitrile (**2**) to form bicyclic pyrimidine derivatives, and that the cyclization proceeds in an electrocyclic manner rather than through a stepwise nucleophilic addition. It thus seemed to be of interest to carry out the cyclization reaction between diaminomethylenehydrazones and **2** in order to examine the nucleophilic behavior of the nitrogens, because the product to be formed should be determined by which of the nitrogens initially attacks **2**. The presence of the more electronegative and smaller nitrogen atom at the 3-position, which corresponds to the sulfur atom in isothiosemicarbazones, may cause the cyclization to occur by an alternative path, such as shown in Chart 1.

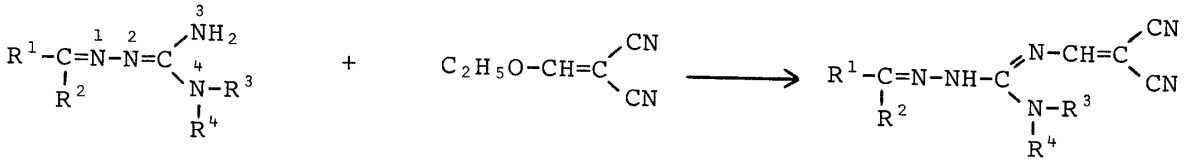
The present paper reports the synthesis and characterization of 5-amino-[1,2,4]triazolo[1,5-*c*]pyrimidine derivatives, as well as the initial condensation product, which is a precursor of these bicyclic pyrimidines, formed by the reaction between diaminomethylenehydrazones bearing up to three substituents on nitrogens and **2**.

Results and Discussion

In a preliminary experiment, amino(dimethylamino)methylenehydrazones (**1a**—**1g**) of

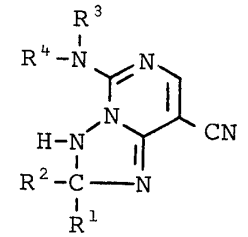
both aromatic aldehydes and ketones were employed for the reaction with **2** in order to restrict the reactive site to N-2 and N-3 and thus to prevent possible side-reactions leading to a complex mixture of products.

The reaction was best performed by heating a solution of **1** and **2** in a molar ratio of 1 : 1.2 in acetonitrile containing triethylamine to reflux temperature (procedure A), giving 43—72% yields of **4** after isolation. If no amine was added in procedure A, the yields diminished to 27—36% and, if R^2 is a methyl group, *i.e.*, the starting diaminomethylenehydrazone is that of a ketone, the reaction did not proceed past the initial condensation stage. When the reaction mixture was left to stand at room temperature (procedure B), **3** was the only product regardless of whether the diaminomethylenehydrazones was that of an aldehyde or ketone. The intermediate product could be converted to the corresponding **4** by heating it, after isolation, under the conditions of procedure A.



1 **2** **3**

	R^1	R^2	R^3	R^4
a:	C_6H_5	H	CH_3	CH_3
b:	*o*-$CH_3OC_6H_4$	H	CH_3	CH_3
c:	*p*-$CH_3OC_6H_4$	H	CH_3	CH_3
d:	*o*-ClC_6H_4	H	CH_3	CH_3
e:	*p*-ClC_6H_4	H	CH_3	CH_3
f:	C_6H_5	CH_3	CH_3	CH_3
g:	*o*-ClC_6H_4	CH_3	CH_3	CH_3
h:	*p*-$CH_3OC_6H_4$	H	$(CH_2)_4$	
i:	*p*-$CH_3OC_6H_4$	CH_3	$(CH_2)_4$	



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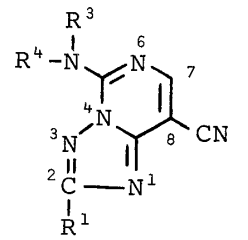

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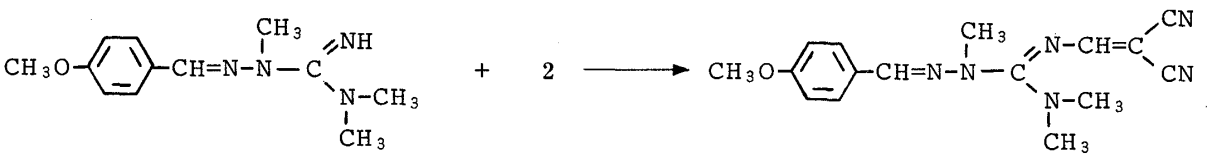
Chart 1

From these results, it is apparent that the reaction of **1** with **2** initially produces **3**, which is then cyclized to **4** under the influence of the tertiary amine, indicating **3** to be a precursor of **4**. When trimethyl compound (**6**), which possesses only a single reactive site at N-3, was treated by procedure A or B, it gave the expected condensation product (**7**) carrying a dicyanovinyl group on the N-3 atom.

The structure of **7** was confirmed on the basis of spectral data, particularly the infrared (IR) spectrum (in KBr pellet), which showed two CN stretching bands at 2230 and 2270 cm^{-1}. The initial condensation products obtained from **1a**—**1g** under the conditions of procedure B invariably showed two CN bands at near 2200 and 2220 cm^{-1} and therefore they should have



6 7

Chart 2

the dicyanovinyl structure proposed in Chart 1. The cyclized product **4** may be formed either by direct cyclization of **3** or through a possible intermediate **8** by stepwise nucleophilic addition. Careful inspection of the reaction mixture did not reveal the presence of **8** in a detectable amount.

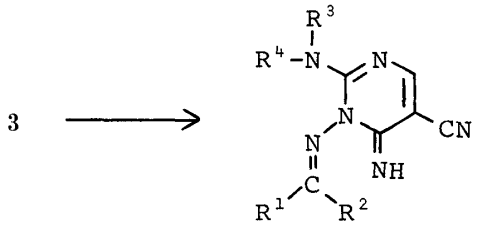


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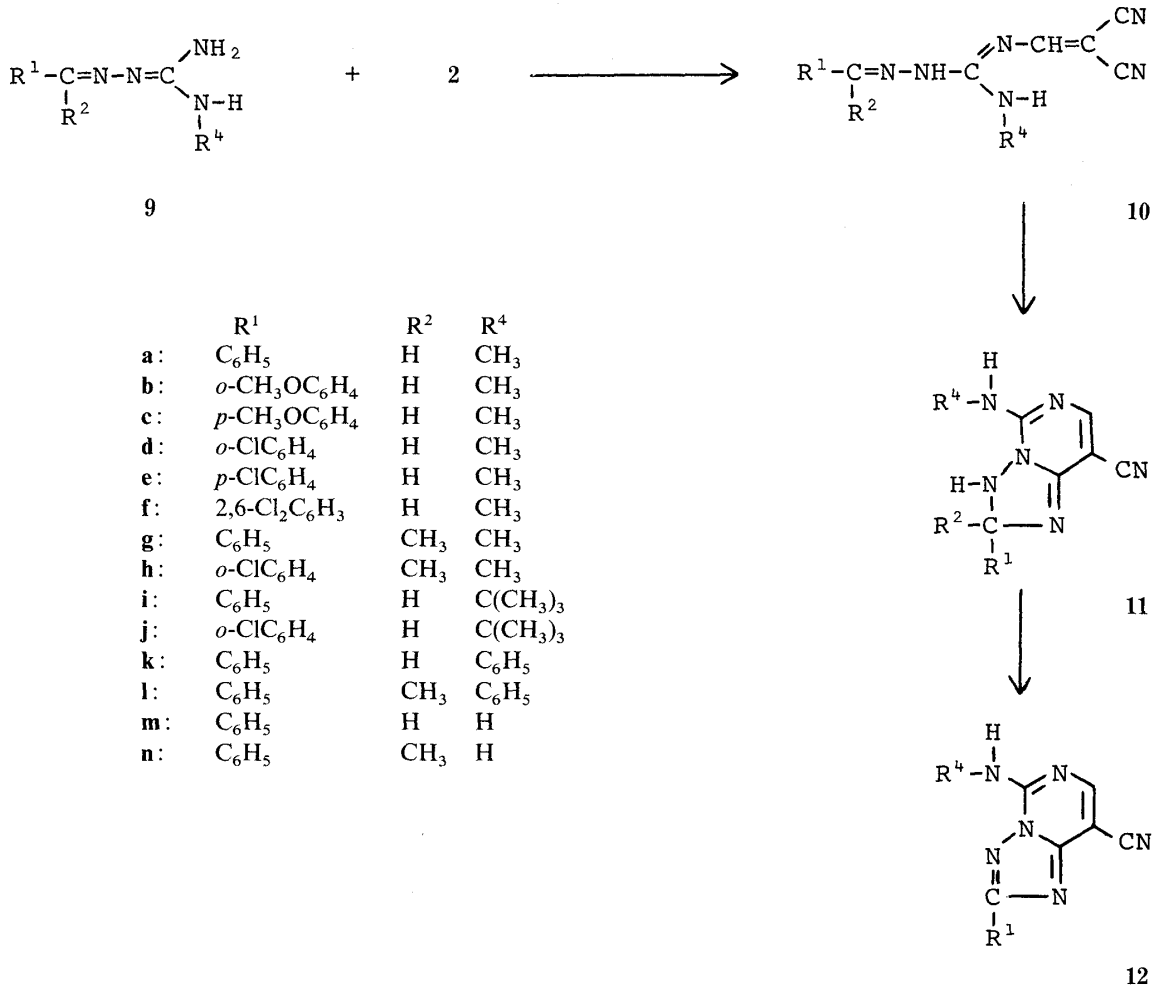
Chart 3

Amino(polymethyleneamino)methylenehydrazones (**1h**, **1i**), which are a class of amino(disubstituted amino)methylenehydrazones, reacted similarly with **2**. When the reaction was carried out by procedure A, however, the products were dependent upon the nature of the carbonyl component of the diaminomethylenehydrazone, *i.e.*, aldehyde diaminomethylenehydrazones ($R^2=H$) were found to give directly the dehydrogenated triazolopyrimidines, while ketone diaminomethylenehydrazones ($R^2=CH_3$) gave the 2,3-dihydro compounds as described above.

Generally, amino(monosubstituted amino)methylenehydrazones were more reactive than amino(disubstituted amino)methylenehydrazones, and reacted so rapidly that the linear intermediate **10** could not be isolated even under mild conditions (procedure B). Diaminomethylenehydrazones having a methyl, *tert*-butyl, or phenyl group on N(4) were compared with one another for their reactivity toward **2** by procedure B. The 4-monomethyl **9a**—**9h** was found to be most reactive and readily gave **11a**—**11h** with high purity. Compounds **9i** and **9j**, in spite of the presence of a sterically bulky group on N(4), reacted smoothly with **2** to give the corresponding **11a**—**11h**. This indicates that the substituents on N(4) offer no steric hindrance to the cyclization of **9** to **11**. Phenylamino compounds (**9k**, **9l**) similarly reacted with **2** to give a mixture of the 2,3-dihydro compound **11k** and the dehydrogenated product **12k**, with the latter being the major component. Thus, the phenyl substituent of N(4) did not prevent the cyclization but accelerated the dehydrogenation of the initially formed dihydro compound **11** to **12**. Consequently, the substituent on N(4) seems to have essentially no effect on the cyclization reaction either sterically or electronically.

Unexpectedly, **9m** and **9n**, which have no substituent on any of N(2) to N(4) showed lower reactivity in the reaction with **2** than did the amino(monosubstituted amino)-methylenehydrazone. Under the conditions of procedure B, **9m** did not cyclize to **11m** but gave **12m** by procedure A. The 2,3-dihydro product **11m** could be obtained only by the



	R^1	R^2	R^4
a:	C_6H_5	H	CH_3
b:	*o*-$CH_3OC_6H_4$	H	CH_3
c:	*p*-$CH_3OC_6H_4$	H	CH_3
d:	*o*-ClC_6H_4	H	CH_3
e:	*p*-ClC_6H_4	H	CH_3
f:	2,6-$Cl_2C_6H_3$	H	CH_3
g:	C_6H_5	CH_3	CH_3
h:	*o*-ClC_6H_4	CH_3	CH_3
i:	C_6H_5	H	$C(CH_3)_3$
j:	*o*-ClC_6H_4	H	$C(CH_3)_3$
k:	C_6H_5	H	C_6H_5
l:	C_6H_5	CH_3	C_6H_5
m:	C_6H_5	H	H
n:	C_6H_5	CH_3	H

Chart 4

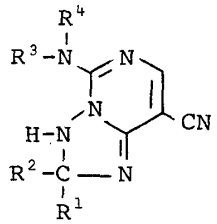
method in which **9m** was heated with **2** at the reflux temperature in acetonitrile.

As described above, aldehyde diaminomethylenehydrazones ($R^2 = H$) can directly cyclize to the corresponding dehydrogenated triazolopyrimidines in the presence of amine in moderate to fairly good yields. However, the dehydrogenation of 2,3-dihydrotriazolopyrimidines could be achieved with iron(III) chloride in aqueous acetic acid (procedure C) or iodine in ethanol at room temperature (procedure D), with yields varying over a wide range.

The structure of the 2,3-dihydro[1,2,4]triazolo[1,5-*c*]pyrimidines and [1,2,4]triazolo[1,5-*c*]pyrimidines have been established on the basis of spectral measurements and elemental analyses.

In the proton nuclear magnetic resonance (^{1}H-NMR) spectra, the 2,3-dihydro structure of 5-(substituted and unsubstituted amino) [1,2,4]triazolo[1,5-*c*]pyrimidines was confirmed by the observation of spin-coupling between H-2 and H-3 protons and the disappearance of H-3 on exchange with deuterium, with simultaneous conversion of the H-2 resonance from a doublet to a singlet. The spectrum of 2-deuterated **4a**-d_1 ($R^2 = D$), which was obtained by using benzaldehyde-d_1 (C_6H_5CDO) amino(dimethylamino)methylenehydrazone (**1a**-d_1) following procedure A, showed the H-3 proton signal as a singlet. The ring proton at the 7-position resonated near δ 7.62—7.76 ($CDCl_3$), which value was not substantially influenced by any structural changes in the remainder of the molecule. The resonance of methyl protons at the 2-position showed an upfield shift by about 0.5 ppm relative to the starting diamino-

TABLE I. 8-Cyano-2,3-dihydro-5-substituted [1,2,4]Triazolo[1,5-*c*]pyrimidines



Compd.	R^1	R^2	R^3	R^4	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found)		
								C	H	N
4a	C_6H_5	H	CH_3	CH_3	49	165—173[a]	$C_{14}H_{14}N_6$	63.14 (62.57	5.30 5.22	31.56 31.66)
4b	*o*-$CH_3OC_6H_4$	H	CH_3	CH_3	63	175—176	$C_{15}H_{14}N_6O$	60.80 (60.60	5.44 5.37	28.36 28.51)
4c	*p*-$CH_3OC_6H_4$	H	CH_3	CH_3	44	136—148[a]	$C_{15}H_{14}N_6O$	60.80 (60.83	5.44 5.42	28.36 28.14)
4d	*o*-ClC_6H_4	H	CH_3	CH_3	63	156—157	$C_{14}H_{13}ClN_6$	55.91 (55.48	4.36 4.29	27.94 27.94)
4e	*p*-ClC_6H_4	H	CH_3	CH_3	43	151—156	$C_{14}H_{13}ClN_6$	55.91 (55.84	4.36 4.29	27.94 28.15)
4f	C_6H_5	CH_3	CH_3	CH_3	60	160—162	$C_{15}H_{16}N_6$	64.27 (63.74	5.75 5.52	29.98 30.02)
4g	*o*-ClC_6H_4	CH_3	CH_3	CH_3	43	176—177	$C_{15}H_{15}ClN_6$	57.22 (57.10	4.80 4.81	26.70 26.91)
4h	*p*-$CH_3OC_6H_4$	H	$(CH_2)_4$		61	161—182[a]	$C_{17}H_{18}N_6O$	63.34 (63.17	5.63 5.52	26.07 25.85)
4i	*p*-$CH_3OC_6H_4$	CH_3	$(CH_2)_4$		54	248—250	$C_{18}H_{20}N_6O$	64.27 (64.31	5.99 6.01	24.98 24.93)

a) Partial oxidation during the course of melting point measurement is presumably responsible for the wide melting range.

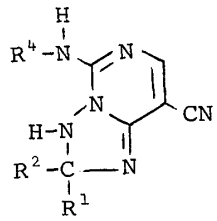
methylenehydrazones, reflecting the structural conversion of the arylmethylene moiety from $-\underset{|}{C}=\underset{|}{N}$ to $-\underset{|}{C}H-\underset{|}{N}-$.

In the mass spectra (MS), molecular ions were obtained for all 2,3-dihydro compounds with an intensity (5—41%) that depended upon the steric crowding at C-2. Abundant ions M^+-R^1 and M^+-R^2 observed in the spectra of 2,3-dihydrotriazolopyrimidines further supported the 2,3-dihydro structure. The fragmentation pathways were confirmed by the MS of the deuterated compounds, **4a**-d_1 and **11a**-d_1, in which R^2 is D. The dehydrogenated compounds showed intense molecular ions (100%) than did the corresponding 2,3-dihydro compounds (5—41%). The fragment ion R^1CN (5—38%) observed in the spectra of dehydrogenated compounds seems to be characteristic of the triazolopyrimidine structure. It provides a means of distinguishing the dehydrogenated compound from the corresponding 2,3-dihydro structure. All of these spectral data support the proposed structures of the 2,3-dihydro and dehydrogenated triazolopyrimidines.

Experimental

Melting points were taken in open glass capillaries and are uncorrected. IR spectra were recorded on a Hitachi EPI-G2 or 260-30 spectrophotometer and calibrated by comparison with that of standard polystyrene film sample. ^{1}H-NMR spectra were obtained with a Hitachi R-24 spectrometer at 60 MHz. Unless otherwise stated, chemical shifts are reported in parts per million (δ scale) downfield from internal tetramethylsilane (TMS). The solvents used

TABLE II. 8-Cyano-2,3-dihydro-5-monosubstituted Amino[1,2,4]triazolo[1,5-*c*]pyrimidines



Compd.	R^1	R^2	R^4	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found)		
							C	H	N
11a	C_6H_5	H	CH_3	48	156—161[a]	$C_{13}H_{12}N_6$	61.89	4.79	33.31
							(61.73	4.72	33.56)
11b	*o*-$CH_3OC_6H_4$	H	CH_3	64	186—189	$C_{14}H_{14}N_6O$	59.56	5.00	29.77
							(59.32	4.91	29.90)
11c	*p*-$CH_3OC_6H_4$	H	CH_3	67	185 200[a]	$C_{14}H_{14}N_6O$	59.56	5.00	29.77
							(59.71	4.97	29.79)
11e	*p*-ClC_6H_4	H	CH_3	63	170—179[a]	$C_{13}H_{11}ClN_6$	54.46	3.87	29.31
							(54.36	3.81	29.14)
11f	2,6-$Cl_2C_6H_3$	H	CH_3	63	186—187	$C_{13}H_{10}Cl_2N_6$	48.62	3.14	26.17
							(48.31	2.91	26.39)
11g	C_6H_5	CH_3	CH_3	53	221—224	$C_{14}H_{14}N_6$	63.14	5.30	31.56
							(63.26	5.28	31.40)
11h	*o*-ClC_6H_4	CH_3	CH_3	20	162—164[b]	$C_{14}H_{13}ClN_6$	55.91	4.36	27.94
							(55.81	4.29	28.24)
11i	C_6H_5	H	$C(CH_3)_3$	65	201—202	$C_{16}H_{18}N_6$	65.29	6.16	28.55
							(64.78	6.03	28.58)
11j	*o*-ClC_6H_4	H	$C(CH_3)_3$	49	171—182[a]	$C_{16}H_{17}ClN_6$	58.45	5.21	25.56
							(58.55	5.19	25.79)
11l	C_6H_5	CH_3	C_6H_5	35	116—117[b]	$C_{19}H_{16}N_6 \cdot 1/2C_2H_5OH$	68.36	5.45	23.91
							(68.48	5.43	24.09)
11m	C_6H_5	H	H	50	185—187	$C_{12}H_{10}N_6$	60.50	4.23	35.27
							(60.23	3.89	35.30)
11n	C_6H_5	CH_3	H	60	255—256	$C_{13}H_{12}N_6$	61.89	4.79	33.31
							(61.73	4.72	33.56)

a) Partial oxidation during the course of melting point measurement is presumably responsible for the wide melting range. *b*) Refluxed in acetonitrile for 3 h.

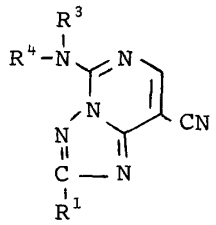
were chloroform-*d* or dimethyl-d_6 sulfoxide for 2,3-dihydro[1,2,4]triazolo[1,5-*c*]pyrimidine compounds and trifluoroacetic acid-*d* for [1,2,4]triazolo[1,5-*c*]pyrimidine compounds. The MS (75 eV) were recorded on a JEOL JMS D100 mass spectrometer.

Benzaldehyde Amino(dimethylamino)methylenehydrazone (1a)——A mixture of benzaldehyde (1.1 g, 0.01 mol), 2-amino-1,1-dimethylguanidine hydriodide (2.3 g, 0.01 mol) and 20 ml of methyl alcohol was acidified with 0.2 ml of concentrated hydrochloric acid. The reaction mixture was allowed to stand at room temperature for 30 min, during which time crystallization of the desired diaminomethylenehydrazone hydriodide was completed. The crystals were collected by filtration and converted to the free base in the usual manner to give pale yellow needles (1.8 g, 98%) with mp 146—148 °C. Recrystallization from isopropyl alcohol did not change the mp or the appearance of the crystals. *Anal.* Calcd for $C_{10}H_{14}N_4$: C, 63.13; H, 7.42; N, 29.45. Found: C, 63.27; H, 7.53; N, 29.39. ^{1}H-NMR ($CDCl_3$) δ: 2.96 [6H, s, $N(CH_3)_2$], 5.20 (2H, s, NH_2), 7.30 (3H, m, phenyl), 7.70 (2H, m, phenyl), 8.20 (1H, s, CH=N).

All the other diaminomethylenehydrazones (**1b**—**1i** and **9a**—**9n**) were prepared similarly and gave appropriate spectral data and satisfactory elemental analyses.

Benzaldehyde 2,2-Dicyanovinylamino(dimethylamino)methylenehydrazone (3a)——A mixture of **1a** (0.19 g, 1 mmol) and **2** (0.15 g, 1.2 mmol) was dissolved in 0.5 ml of acetonitrile and the reaction mixture was allowed to stand at room temperature. After standing for 30 min, crystals gradually deposited from the solution, and were collected by filtration to give 0.1 g (38%) of analytically pure **3a** as pale yellow needles with mp 158—159 °C. *Anal.* Calcd for

TABLE III. 8-Cyano-5-substituted [1,2,4]Triazolo[1,5-*c*]pyrimidines



Compd.	R^1	R^3	R^4	Yield (%)	mp (°C)	Procedure	Formula	Analysis (%) Calcd (Found)		
								C	H	N
5a	C_6H_5	CH_3	CH_3	34	204—206	C	$C_{14}H_{12}N_6$	63.63	4.58	31.80
								(63.40	4.58	31.73)
5b	*o*-$CH_3OC_6H_4$	CH_3	CH_3	31	218—224	C	$C_{15}H_{14}N_6O$	61.22	4.79	28.55
								(61.10	4.19	28.72)
5c	*p*-$CH_3OC_6H_4$	CH_3	CH_3	68	180—190	C	$C_{15}H_{14}N_6O$	61.22	4.79	28.55
								(61.19	4.77	28.37)
5d	*o*-ClC_6H_4	CH_3	CH_3	64	205—209	C	$C_{14}H_{11}ClN_6$	56.29	3.71	28.13
								(56.04	3.50	28.33)
5e	*p*-ClC_6H_4	CH_3	CH_3	56	239—249	C	$C_{14}H_{11}ClN_6$	56.29	3.71	28.13
								(56.36	3.57	28.38)
5h	*p*-$CH_3OC_6H_4$	$(CH_2)_4$		40	250—252	*a)*	$C_{17}H_{16}N_6O$	63.74	5.03	26.23
								(63.52	5.02	26.22)
12a	C_6H_5	H	CH_3	67	232—234	D	$C_{13}H_{10}N_6$	62.39	4.03	33.58
								(62.29	3.99	33.27)
12b	*o*-$CH_3OC_6H_4$	H	CH_3	42	200—201	D	$C_{14}H_{12}N_6O$	59.99	4.31	29.98
								(59.85	4.13	30.02)
12c	*p*-$CH_3OC_6H_4$	H	CH_3	64	263—266	D	$C_{14}H_{12}N_6O$	59.99	4.31	29.98
								(59.88	4.26	29.82)
12d	*o*-ClC_6H_4	H	CH_3	28	180—181	D	$C_{13}H_9ClN_6$	54.84	3.19	29.52
								(54.58	3.00	29.34)
12e	*p*-ClC_6H_4	H	CH_3	28	234—235	D	$C_{13}H_9ClN_6$	54.84	3.19	29.52
								(54.73	3.09	29.65)
12f	2,6-$Cl_2C_6H_3$	H	CH_3	29	243—245	D	$C_{13}H_8Cl_2N_6$	48.92	2.53	26.33
								(48.67	2.37	26.05)
12i	C_6H_5	H	$C(CH_3)_3$	48	215—216	D	$C_{16}H_{16}N_6$	65.74	5.52	28.75
								(65.78	5.46	28.60)
12j	*p*-$CH_3OC_6H_4$	H	$C(CH_3)_3$	26	218—222	*a)*	$C_{17}H_{18}N_6O$	63.34	5.63	26.07
								(63.48	5.57	25.93)
12k	C_6H_5	H	C_6H_5	20	225—226	*a)*	$C_{18}H_{12}N_6$	69.22	3.87	26.91
								(69.11	3.71	26.77)
12m	C_6H_5	H	H	68	279—280	*a)*	$C_{12}H_8N_6$	61.01	3.41	35.57
								(60.79	3.26	35.57)

a) A solution of **9** and **2** in acetonitrile containing triethylamine was allowed to stand at room temperature for 3 d.

$C_{14}H_{14}N_6$: C, 63.14; H, 5.30; N, 31.56. Found: C, 62.80; H, 5.20; N, 31.71. IR ν_{max}^{KBr} cm^{-1}: 2200, 2210 (CN). ^{1}H-NMR (DMSO-d_6) δ: 3.17 [6H, s, $N(CH_3)_2$], 7.48 (6H, m, phenyl), 8.08 (1H, s, C=CH), 8.27 (1H, s, CH=N), 11.25 (1H, s, NH). MS *m/e*: 266 (M^+), 264 (M^+-2H), 189 ($M^+-C_6H_5$), 103 (C_6H_5CN).

The following dicyanovinyl compounds were prepared similarly.

Acetophenone 2,2-Dicyanovinylamino(dimethylamino)methylenehydrazone (**3f**): Pale yellow needles (from methyl alcohol), mp 150—151 °C. *Anal.* Calcd for $C_{15}H_{16}N_6$: C, 64.27; H, 5.75: N, 29.98. Found: C, 64.06; H, 5.73; N, 29.84. IR ν_{max}^{KBr} cm^{-1}: 2140, 2180 (CN). ^{1}H-NMR (DMSO-d_6) δ: 2.37 (3H, s, CH_3), 3.14 [6H, s, $N(CH_3)_2$], 7.37 (3H, m, phenyl), 7.22 (2H, m, phenyl), 8.07 (1H, s, CH), 9.90 (2H, s, NH_2). MS *m/e*: 280 (M^+), 265 (M^+-CH_3).

o-Chlorobenzaldehyde 2,2-Dicyanovinylamino(dimethylamino)methylenehydrazone (**10d**): Pale yellow needles,

TABLE IV. Spectral Data for 8-Cyano-2,3-dihydro[1,2,4]triazolo[1,5-*c*]pyrimidines

Compd.	IR (KBr) cm^{-1}	^{1}H-NMR spectra δ/ppm (from TMS in DMSO-d_6)			MS *m/e* (rel. int.)		
	CN	H-2 (*J*)	H-3 (*J*)	H-7	M^+	M^+-R^1	M^+-R^2
4a	2200	6.00 (12)	5.10 (12)	7.63[a]	266 (19)	189 (34)	265 (17)
4a-d_1	2200	—	5.10	7.64[a]	267 (23)	190 (42)	265 (15)
4b	2200	6.68 (11)	6.18 (11)	7.85	296 (16)	189 (23)	295 (24)
4c	2200	5.93 (12)	5.08 (12)	7.63[a]	296 (22)	189 (14)	295 (17)
4d	2200	6.95 (11)	6.26 (11)	7.92	300 (30)	189 (16)	299 (29)
4e	2200	6.01 (12)	5.40 (12)	7.62[a]	300 (29)	189 (23)	299 (19)
4f	2200	1.71[b]	4.67	7.63[a]	280 (14)	203 (19)	265 (100)
4g	2200	1.89[b]	4.67	7.76[a]	314 (5)	203 (24)	293 (100)
4h	2200	6.55 (11)	5.86 (11)	7.80	322 (9)	216 (6)	321 (18)
4i	2200	1.57[b]	6.41	7.80	336 (5)	229 (7)	321 (86)
11a	2210	6.52 (10.4)	6.09 (10.4)	7.88	252 (26)	175 (100)	251 (34)
11a-d_1	2200	—	6.09	7.89	253 (22)	176 (100)	251 (10)
11b	2200	6.55 (10.4)	6.32 (10.4)	7.90	282 (20)	175 (100)	281 (20)
11c	2200	6.42 (10.4)	6.05 (10.4)	7.90	282 (39)	175 (61)	281 (73)
11e	2200	6.68 (10.4)	6.18 (10.4)	7.92	286 (39)	175 (81)	285 (36)
11f	2200	7.45 (8.8)	7.13 (8.8)	7.98	320 (6)	175 (1)	319 (1)
11g	2200	1.67[b]	6.30	7.89	266 (13)	189 (50)	251 (100)
11h	2200	1.80[b]	6.50	7.90	300 (5)	189 (35)	285 (100)
11i	2200	6.42 (11)	6.02 (11)	7.86	294 (29)	217 (20)	293 (9)
11j	2200	6.32 (11)	6.00 (11)	7.90	328 (15)	217 (11)	327 (1)
11l	2200	1.70[b]	4.75	7.75	328 (11)	251 (26)	313 (100)
11m	2200	6.60 (10.4)	6.10 (10.4)	7.79	238 (41)	237 (41)	237 (50)
11n	2210	1.65[b]	6.30	7.78	252 (11)	175 (20)	237 (100)

a) In $CDCl_3$. *b*) Methyl protons.

TABLE V. Spectral Data for 8-Cyano[1,2,4]triazolo[1,5-*c*]pyrimidines

Compd.	IR (KBr) cm^{-1}	^{1}H-NMR (CF_3COOD) δ	MS *m/e* (rel. int.)		
	CN	H-7	M^+	R^1CN	$R^1\overset{+}{C}NH$
5a	2210	8.49	264 (100)	103 (10)	104 (12)
5b	2220	8.78	294 (9)	133 (24)	134 (60)
5c	2220	8.05	294 (100)	133 (13)	134 (13)
5d	2220	8.75	298 (100)	137 (11)	138 (10)
5e	2210	8.81	298 (100)	137 (14)	138 (10)
5h	2200	8.20	320 (60)	133 (8)	—
12a	2210	8.90	250 (100)	103 (9)	104 (23)
12b	2220	8.92	280 (58)	133 (21)	134 (15)
12c	2230	8.90	280 (100)	133 (25)	134 (19)
12d	2230	8.56[a]	284 (100)	137 (7)	138 (11)
12e	2220	8.94	284 (100)	137 (10)	138 (12)
12f	2230	8.90	315 (55)	171 (1)	172 (1)
12i	2200	8.40	292 (23)	103 (7)	104 (14)
12j	2200	8.52[a]	322 (17)	133 (7)	134 (9)
12k	2210	8.75	312 (100)	103 (5)	104 (8)
12m	2230	8.78	236 (100)	103 (7)	104 (17)

a) In DMSO-d_6.

mp 149—151 °C. *Anal.* Calcd for $C_{13}H_{11}ClN_6 \cdot 1/2H_2O$: C, 52.79; H, 4.09; N, 28.41. Found: C, 53.00; H, 3.74; N, 28.64. IR ν_{max}^{KBr} cm^{-1}: 2200, 2210 (CN). ^{1}H-NMR (DMSO-d_6) δ: 2.95 (3H, d, J=5.4 Hz, NHC$\underline{H}_3$), 7.21—7.55 (3H, m, aromatic), 8.35 (1H, s, N–CH=), 8.61 (1H, s, CH=N). MS *m/e*: 286 (M^+), 183 (M^+–C_6H_5CN).

o-Chloroacetophenone 2,2-Dicyanovinylamino(dimethylamino)methylenehydrazone (**10h**): Pale yellow needles, mp 139—141 °C. *Anal.* Calcd for $C_{14}H_{13}ClN_6$: C, 55.91; H, 4.36; N, 27.95. Found: C, 55.68; H, 4.32; N, 27.71. IR ν_{max}^{KBr} cm^{-1}: 2200, 2230 (CN). ^{1}H-NMR (DMSO-d_6) δ: 2.37 (3H, s, CH_3), 2.85 (3H, d, J=3.0 Hz, NHC$\underline{H}_3$), 7.30—7.50 (3H, m, aromatic), 7.80—8.10 (1H, m, aromatic), 8.15 (1H, s, CH). MS *m/e*: 300 (M^+).

p-Methoxyacetophenone 2,2-Dicyanovinylamino(dimethylamino)methylenemethylhydrazone (**7**): Pale yellow prisms (from acetonitrile), mp 180—182 °C. *Anal.* Calcd for $C_{16}H_{18}N_6O$: C, 61.92; H, 5.85; N, 27.08. Found: C, 61.92; H, 5.80; N, 27.14. IR ν_{max}^{KBr} cm^{-1}: 2230, 2270 (CN). ^{1}H-NMR (DMSO-d_6) δ: 3.12 [6H, s, $N(CH_3)_2$], 3.35 (3H, s, NCH_3), 3.82 (3H, s, OCH_3), 6.92 (2H, d, J=9.6 Hz, aromatic), 7.63 (2H, d, J=9.6 Hz, aromatic), 7.90 (1H, s, CH=C), 8.00 (1H, s, CH=N). MS *m/e*: 310 (M^+).

8-Cyano-5-dimethylamino-2,3-dihydro-2-phenyl[1,2,4]triazolo[1,5-*c*]pyrimidine (4a)——Procedure A: A mixture of **1a** (0.19 g, 1 mmol), **2** (0.15 g, 1.2 mmol), and 0.5 ml of acetonitrile containing 0.1 ml of triethylamine was heated under reflux for 5 min. The reaction mixture was evaporated to give a crude product as a brown oil. The residual oil was crystallized from isopropyl alcohol and the crystals formed were collected by filtration to give 0.13 g (49%) of analytically pure **4a** as pale yellow needles, mp 165—173 °C. *Anal.* Calcd for $C_{14}H_{14}N_6$: C, 63.14; H, 5.30; N, 31.56. Found: C, 62.57; H, 5.22; N, 31.30. IR ν_{max}^{KBr} cm^{-1}: 3170, 2920 (NH), 2200 (CN). ^{1}H-NMR ($CDCl_3$) δ: 3.24 [6H, s, $N(CH_3)_2$], 5.10 (1H, d, J=12.0 Hz, NH), 6.00 (1H, d, J=12.0 Hz, CH), 7.35 (5H, m, phenyl), 7.62 (1H, s, H-7). MS *m/e*: 266 (M^+), 264 (M^+-2H), 189 ($M^+ - C_6H_5$).

8-Cyano-2,3-dihydro-5-methylamino-2-phenyl[1,2,4]triazolo[1,5-*c*]pyrimidine (11a)——Procedure B: A mixture of **9a** (0.18 g, 1 mmol) and **2** (0.15 g, 1.2 mmol) was dissolved in 0.5 ml of acetonitrile and the reaction mixture was allowed to stand at room temperature. After 1 h, crystals gradually deposited from the solution, and were collected by filtration to give 0.12 g (48%) of analytically pure **11a** as pale yellow needles with mp 156—161 °C. *Anal.* Calcd for $C_{13}H_{12}N_6$: C, 61.89; H, 4.79; N, 33.31. Found: C, 61.73; H, 4.72; N, 33.56. IR ν_{max}^{KBr} cm^{-1}: 3180, 3240 (NH), 2210 (CN). ^{1}H-NMR (DMSO-d_6) δ: 2.32 (3H, d, J=4.0 Hz, NHCH), 6.09 (1H, d, J=10.4 Hz, H-3), 6.52 (1H, d, J=10.4 Hz, H-2), 7.33 (5H, s, phenyl), 7.88 (1H, s, H-7). MS *m/e*: 252 (M^+), 175 ($M^+ - C_6H_5$), 103 (C_6H_5CN).

8-Cyano-5-dimethylamino-2-phenyl[1,2,4]triazolo[1,5-*c*]pyrimidine (5a)——Procedure C: A solution of 1 mmol of iron(III) chloride in 1 ml of water was added to a solution of **4a** (0.13 g, 0.5 mmol) in 1 ml of a mixture of acetonitrile, acetic acid and water in 2 : 1 : 1 by volume, and the resulting cloudy solution was allowed to stand overnight at room temperature. The reaction mixture was diluted with sufficient water to precipitate completely the oxidized product, which was collected by filtration to give 0.09 g (34%) of analytically pure product as colorless needles, mp 205—206 °C. *Anal.* Calcd for $C_{14}H_{12}N_6$: C, 63.63; H, 4.58; N, 31.80. Found: C, 63.40; H, 4.58; N, 31.73. IR ν_{max}^{KBr} cm^{-1}: 2220 (CN). ^{1}H-NMR (CF_3COOD) δ: 3.62 [6H, s, $N(CH_3)_2$], 7.58 (3H, m, phenyl), 8.19 (2H, m, phenyl), 8.49 (1H, s, H-7). MS *m/e*: 264 (M^+).

8-Cyano-5-methylamino-2-phenyl[1,2,4]triazolo[1,5-*c*]pyrimidine (12a)——Procedure D: A solution (3.5 ml) containing 1 mmol/5 ml of iodine in ethyl alcohol (0.7 mmol) was added to a solution of **11a** (0.1 g, 0.4 mmol) in acetonitrile (1 ml), and the mixture was allowed to stand at room temperature with occasional agitation for 1 d. The reaction mixture was then diluted with sufficient water to precipitate completely the oxidized product, which was collected by filtration to give 0.05 g (50%) of analytically pure **12a** as pale yellow needles, mp 232—234 °C. *Anal.* Calcd for $C_{13}H_{10}N_6$: C, 62.39; H, 4.03; N, 33.58. Found: C, 62.29; H, 3.99; N, 33.29. IR ν_{max}^{KBr} cm^{-1}: 3300 (NH), 2210 (CN). ^{1}H-NMR (CF_3COOD) δ: 3.53 (3H, s, CH_3), 7.72 (3H, m, phenyl), 8.15 (2H, m, phenyl), 8.90 (1H, s, H-7). MS *m/e*: 250 (M^+), 249 ($M^+ - 1$), 147 ($M^+ - C_6H_5CN$).

5-Amino-8-cyano-2-phenyl[1,2,4]triazolo[1,5-*c*]pyrimidine (12m)——A mixture of **9m** (0.16 g, 1 mmol), **2** (0.15 g, 1.2 mmol) and 1 ml of acetonitrile containing 0.1 ml of triethylamine was allowed to stand at room temperature. After 3 d, crystals gradually deposited from the solution, and were collected by filtration to give 0.16 g (68%) of the desired product as yellow crystals with mp 279—280 °C. Recrystallization from ethyl alcohol gave pale yellow needles, mp 279—280 °C. *Anal.* Calcd for $C_{12}H_8N_6$: C, 61.01; H, 3.41; N, 35.57. Found: C, 60.76; H, 3.26; N, 35.29. IR ν_{max}^{KBr} cm^{-1}: 3460 (NH), 2230 (CN). ^{1}H-NMR (CF_3COOD) δ: 7.68 (3H, m, phenyl), 8.20 (2H, m, phenyl), 8.78 (1H, s, H-7). MS *m/e*: 236 (M^+), 235 ($M^+ - 1$), 104 ($C_6H_5CN^+H$).

Conversion of 3f to 4f——A solution of **3f** (0.2 g) and triethylamine (0.1 ml) in a mixture of acetonitrile and methyl alcohol (1 : 1 by volume) (1 ml) was refluxed for 10 min and then evaporated. The residue was crystallized from methyl alcohol to give **4f** as pale yellow needles (0.15 g, 75%), mp 160—161 °C, not depressed upon admixture with the product obtained by direct cyclization of **1f** with **2**.

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